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APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

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- Descriptive title of the Invention
- Cross References to Related Applications
- Statement Regarding Fed sponsored R & D
- Reference to Microfiche Appendix
- Background of the Invention
- Brief Summary of the Invention
- Brief Description of the Drawings (if filed)
- Detailed Description
- Claim(s)
- Abstract of the Disclosure

3. ☒ Drawing(s) (35 USC 113) [Total Sheets 11]

4. Oath or Declaration [Total Pages 2]
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METHOD AND APPARATUS FOR A MULTIPLE PART
CAPILLARY DEVICE FOR USE IN MASS SPECTROMETRY

TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to mass spectrometry and the analysis of chemical samples, and more particularly to capillaries for use in mass spectrometry. Described herein is a multiple part capillary for use in mass spectrometry (particularly with ionization sources) to transport ions from an ionization source to subsequent regions of a mass spectrometer for analysis therein.

BACKGROUND OF THE PRESENT INVENTION

The present invention relates to capillary tubes for use in mass spectrometry. Mass spectrometry is an important tool in the analysis of a wide range of chemical compounds. Specifically, mass spectrometers can be used to determine the molecular weight of sample compounds. The analysis of samples by mass spectrometry consists of three main steps -- formation of ions from sample material, mass analysis of the ions to separate the ions from one another according to ion mass, and detection of the ions. A variety of means exist in the field of mass spectrometry to perform

1 each of these three functions. The particular combination of means
2 used in a given spectrometer determine the characteristics of that
3 spectrometer.

4 To mass analyze ions, for example, one might use a magnetic
5 (B) or electrostatic (E) analyzer. Ions passing through a magnetic
6 or electrostatic field will follow a curved path. In a magnetic
7 field the curvature of the path will be indicative of the momentum-
8 to-charge ratio of the ion. In an electrostatic field, the
9 curvature of the path will be indicative of the energy-to-charge
10 ratio of the ion. If magnetic and electrostatic analyzers are used
11 consecutively, then both the momentum-to-charge and energy-to-
12 charge ratios of the ions will be known and the mass of the ion
13 will thereby be determined. Other mass analyzers are the
14 quadrupole (Q), the ion cyclotron resonance (ICR), the time-of-
15 flight (TOF), and the quadrupole ion trap analyzers.

16 Before mass analysis can begin, however, gas phase ions must
17 be formed from sample material. If the sample material is
18 sufficiently volatile, ions may be formed by electron ionization
19 (EI) or chemical ionization (CI) of the gas phase sample molecules.
20 For solid samples (e.g. semiconductors, or crystallized
21 materials), ions can be formed by desorption and ionization of

1 sample molecules by bombardment with high energy particles.
2 Secondary ion mass spectrometry (SIMS), for example, uses keV ions
3 to desorb and ionize sample material. In the SIMS process a large
4 amount of energy is deposited in the analyte molecules. As a
5 result, fragile molecules will be fragmented. This fragmentation
6 is undesirable in that information regarding the original
7 composition of the sample -- e.g., the molecular weight of sample
8 molecules -- will be lost.

9 For more labile, fragile molecules, other ionization methods
10 now exist. The plasma desorption (PD) technique was introduced by
11 Macfarlane et al. in 1974 (Macfarlane, R. D.; Skowronski, R. P.;
12 Torgerson, D. F., *Biochem. Biophys. Res Commoun.* 60 (1974) 616).
13 Macfarlane et al. discovered that the impact of high energy (MeV)
14 ions on a surface, like SIMS would cause desorption and ionization
15 of small analyte molecules, however, unlike SIMS, the PD process
16 results also in the desorption of larger, more labile species --
17 e.g., insulin and other protein molecules.

18 Lasers have been used in a similar manner to induce desorption
19 of biological or other labile molecules. See, for example,
20 VanBreeman, R.B.; Snow, M.; Cotter, R.J., *Int. J. Mass Spectrom.*
21 *Ion Phys.* 49 (1983) 35; Tabet, J.C.; Cotter, R.J., *Anal. Chem.* 56

1 (1984) 1662; or Olthoff, J.K.; Lys, I.; Demirev, P.: Cotter, R.
2 J., *Anal. Instrument.* 16 (1987) 93. Cotter et al. modified a CVC
3 2000 time-of-flight mass spectrometer for infrared laser desorption
4 of involatile biomolecules, using a Tachisto (Needham, Mass.) model
5 215G pulsed carbon dioxide laser. The plasma or laser desorption
6 and ionization of labile molecules relies on the deposition of
7 little or no energy in the analyte molecules of interest. The use
8 of lasers to desorb and ionize labile molecules intact was enhanced
9 by the introduction of matrix assisted laser desorption ionization
10 (MALDI) (Tanaka, K.; Waki, H.; Ido, Y.; Akita, S.; Yoshida, Y.;
11 Yoshica, T., *Rapid Commun. Mass Spectrom.* 2 (1988) 151 and Karas,
12 M.; Hillenkamp, F., *Anal. Chem.* 60 (1988) 2299). In the MALDI
13 process, an analyte is dissolved in a solid, organic matrix. Laser
14 light of a wavelength that is absorbed by the solid matrix but not
15 by the analyte is used to excite the sample. Thus, the matrix is
16 excited directly by the laser, and the excited matrix sublimates into
17 the gas phase carrying with it the analyte molecules. The analyte
18 molecules are then ionized by proton, electron, or cation transfer
19 from the matrix molecules to the analyte molecules. This process,
20 MALDI, is typically used in conjunction with time-of-flight mass
21 spectrometry (TOFMS) and can be used to measure the molecular

1 weights of proteins in excess of 100,000 daltons.

2 Atmospheric pressure ionization (API) includes a number of
3 methods. Typically, analyte ions are produced from liquid solution
4 at atmospheric pressure. One of the more widely used methods,
5 known as electrospray ionization (ESI), was first suggested by Dole
6 et al. (M. Dole, L.L. Mack, R.L. Hines, R.C. Mobley, L.D. Ferguson,
7 M.B. Alice, *J. Chem. Phys.* 49, 2240, 1968). In the electrospray
8 technique, analyte is dissolved in a liquid solution and sprayed
9 from a needle. The spray is induced by the application of a
10 potential difference between the needle (where the liquid emerges)
11 and a counter electrode. By subjecting the emerging liquid to a
12 strong electric field, it becomes charged, and as a result, it
13 "breaks up" into smaller particles if the charge imposed on the
14 liquid's surface is strong enough to overcome the surface tension
15 of the liquid (i.e., as the particles attempt to disperse the
16 charge and return to a lower energy state). This results in the
17 formation of finely charged droplets of solution containing analyte
18 molecules. These droplets further evaporate leaving behind bare
19 charged analyte ions.

20 Electrospray mass spectrometry (ESMS) was introduced by
21 Yamashita and Fein (M. Yamashita and M.B. Fein, *J. Phys. Chem.* 88,

1 4671, 1984). To establish this combination of ESI and MS, ions had
2 to be formed at atmospheric pressure, and then introduced into the
3 vacuum system of a mass analyzer via a differentially pumped
4 interface. The combination of ESI and MS afforded scientists the
5 opportunity to mass analyze a wide range of samples, and ESMS is
6 now widely used primarily in the analysis of biomolecules (e.g.
7 proteins) and complex organic molecules.

8 In the intervening years a number of means and methods useful
9 to ESMS and API-MS have been developed. Specifically, much work
10 has focused on sprayers and ionization chambers. In addition to
11 the original electrospray technique, pneumatic assisted
12 electrospray, dual electrospray, and nano electrospray are now also
13 widely available. Pneumatic assisted electrospray (A.P. Bruins,
14 T.R. Covey, and J.D. Henion, *Anal. Chem.* 59, 2642, 1987) uses
15 nebulizing gas flowing past the tip of the spray needle to assist
16 in the formation of droplets. The nebulization gas assists in the
17 formation of the spray and thereby makes the operation of ESI
18 easier. Nano electrospray (M.S. Wilm, M. Mann, *Int. J. Mass*
19 *Spectrom. Ion Processes* 136, 167, 1994) employs a much smaller
20 diameter needle than the original electrospray. As a result the
21 flow rate of sample to the tip is lower and the droplets in the

1 spray are finer. However, the ion signal provided by nano
2 electrospray in conjunction with MS is essentially the same as with
3 the original electrospray. Nano electrospray is therefore much
4 more sensitive with respect to the amount of material necessary to
5 perform a given analysis.

6 Many other ion production methods might be used at atmospheric
7 or elevated pressure. For example, MALDI has recently been adapted
8 by Victor Laiko and Alma Burlingame to work at atmospheric pressure
9 (Atmospheric Pressure Matrix Assisted Laser Desorption Ionization,
10 poster #1121, 4th International Symposium on Mass Spectrometry in
11 the Health and Life Sciences, San Francisco, Aug. 25 - 29, 1998)
12 and by Standing et al. at elevated pressures (Time of Flight Mass
13 Spectrometry of Biomolecules with Orthogonal Injection +
14 Collisional Cooling, poster #1272, 4th International Symposium on
15 Mass Spectrometry in the Health and Life Sciences, San Francisco,
16 Aug. 25 - 29, 1998; and Orthogonal Injection TOFMS *Anal. Chem.*
17 71(13), 452A (1999)). The benefit of adapting ion sources in this
18 manner is that the ion optics and mass spectral results are largely
19 independent of the ion production method used.

20 An elevated pressure ion source always has an ion production
21 region (wherein ions are produced) and an ion transfer region

1 (wherein ions are transferred through differential pumping stages
2 and into the mass analyzer). The ion production region is at an
3 elevated pressure -- most often atmospheric pressure -- with
4 respect to the analyzer. The ion production region will often
5 include an ionization "chamber". In an ESI source, for example,
6 liquid samples are "sprayed" into the "chamber" to form ions.

7 The design of the ionization chamber used in conjunction with
8 API-MS has had a significant impact on the availability and use of
9 these ionization methods with MS. Prior art ionization chambers
10 are inflexible to the extent that a given ionization chamber can be
11 used readily with only a single ionization method and a fixed
12 configuration of sprayers. For example, in order to change from a
13 simple electrospray method to a nano electrospray method of
14 ionization, one had to remove the electrospray ionization chamber
15 from the source and replace it with a nano electrospray chamber
16 (see also, Gourley et al. United States Pat. No. 5,753,910,
17 entitled Angled Chamber Seal for Atmospheric Pressure Ionization
18 Mass Spectrometry). In a co-pending application, entitled,
19 Ionization Chamber For Atmospheric Pressure Ionization, this
20 problem is addressed by disclosing an API ionization chamber
21 providing multiple ports for employing multiple devices in a

1 variety of combinations (e.g., any type of sprayer, lamp,
2 microscope, camera or other such device in various combinations).
3 Further, any given sprayer may produce ions in a manner that is
4 synchronous or asynchronous with the spray from any or all of the
5 other sprayers. By spraying in an asynchronous manner, analyte
6 from a multitude of inlets may be sampled in a multiplexed manner.

7 Analyte ions produced via an API method need to be transported,
8 from the ionization region through regions of differing pressures
9 and ultimately to a mass analyzer for subsequent analysis (e.g.,
10 via time-of-flight mass spectrometry (TOFMS), Fourier transform
11 mass spectrometry (FTMS), etc.). In prior art sources, this was
12 accomplished through use of a small orifice or capillary tube
13 between the ionization region and the vacuum region. An example of
14 such a prior art capillary tube is shown in FIG. 1. As depicted,
15 capillary 7 comprises a generally cylindrical glass tube 2 having
16 an internal bore 4. The ends of capillary 7 include a metal
17 coating (e.g., platinum, copper, etc.) to form conductors 5 which
18 encompass the outer surface of capillary 7 at its ends, leaving a
19 central aperture 6 such that the entrance and exit to internal bore
20 3 are left uncovered. Conductors 5 may be connected to electrical
21 contacts (not shown) in order to maintain a desired space potential

1 at each end of capillary 7. In operation, a first electrode (one
2 of conductors 5) of capillary 7 may be maintained at an extreme
3 negative potential (e.g. -4,500V), while the other electrode (the
4 other of conductors 5), which may form the first stage of a multi-
5 stage lensing system for the final direction of the ions to the
6 spectrometer, may be maintained at a positive potential (e.g., 160
7 volts.

8 It is often observed that the capillaries used in MS analysis
9 acquire deposits over time. Therefore, through normal operation
10 the capillaries need to be regularly cleaned or even replaced. To
11 do so, the MS system must be turned off before the capillary can be
12 removed -- requiring the pumps to be shut down and the vacuum
13 system to be broken -- thereby rendering the system unavailable for
14 hours and even days at a time.

15 More recently, Lee et al. U.S. Pat. No. 5,965,883 attempted to
16 solve this problem in the manner shown by FIG. 2. Shown in FIG. 2
17 is capillary 8 which comprises an outer capillary sleeve 9
18 surrounding an inner capillary tube 10. Sleeve 9 has substantially
19 cylindrical inner surface 11 and outer surface 14. Similarly, tube
20 10 has substantially cylindrical inner surface 12 and outer surface
21 13. The innermost channel, or bore, of capillary 8 is

1 substantially formed by inner surface 12 of tube 10. Capillary 8
2 is substantially radially symmetrical about its central
3 longitudinal axis 15 extending from an upstream end 16 to a
4 downstream end 17. At each end, capillary 8 has conductive end
5 caps 18 comprising the unitary combination of a tubular body having
6 cylindrical inner surface 20 and outer surface 21 and an end plate
7 22 having inner surface 23 and outer surface 24 with a central
8 aperture. The tubular body of end cap 18 encompasses and is in
9 circumferential engagement with a reduced diameter portion 25 of
10 sleeve 9 adjacent to the respective ends of capillary 8, such that
11 the external diameter of end cap 18 substantially the same as the
12 external diameter of sleeve outer surface 14.

13 In order to remove tube 10, end cap 18 at the upstream end of
14 capillary 8 is first removed. A removal tool (not shown) is
15 inserted into the tube as to engage the tube's inner surface 12.
16 It is further suggested by the prior art that in order to remove
17 tube 10 it may be necessary to apply a slight torque orthogonal to
18 axis 15, or other appropriate means such as bonding a removal tool
19 to the tube using an adhesive. Once the tube is withdrawn, a
20 replacement tube may be inserted into sleeve 9. However, this too
21 is difficult and cumbersome, requiring tools to remove and replace

1 the inner capillary tube.

2 Such prior art designs for the transfer capillary have
3 inherent limitations relating to geometry, orientation, and ease of
4 use. The capillary according to these prior art designs is
5 substantially fixed in the source. Only if the instrument -- or at
6 least the source -- is vented to atmospheric pressure can the
7 capillary be removed. The geometric relation of the capillary is
8 therefore fixed with respect to the source and all its components.
9 This implies that the ion production means - e.g. an electrospray
10 needle, atmospheric pressure chemical ionization sprayer, or MALDI
11 probe - must be positioned with respect to the capillary entrance.
12 In order to change from one ion production means to another - e.g.
13 from an electrospray needle to a nano electrospray needle - the
14 first means must be removed from the vicinity of the capillary
15 entrance and the second must then be properly positioned with
16 respect to the capillary entrance. For any production means, there
17 will be an optimum geometry between the means and the capillary
18 entrance at which the ion current passing into the analyzer is
19 maximized. To achieve this optimum, a positioning means must be
20 provided for positioning the ion production means with respect to
21 the capillary entrance. This might take the form of precision

1 machined components, a translation stage on which the ion
2 production means is mounted, or some other device. If the ion
3 production means is required or desired to be remote from the
4 source, a long, fixed length capillary would have to be produced
5 and installed (in a fixed position) in the source.

6 Another limitation of prior art capillaries relates to the
7 orientation of the capillary bore with respect to the ion
8 production means. Such orientation can be important for the
9 operation of the source. One major consideration in the operation
10 of an electrospray source is the formation of large droplets from
11 the analyte solution at the spray needle. Such droplets do not
12 readily evaporate. If these droplets enter the capillary, they may
13 cause the capillary to become contaminated with a residue of
14 analyte molecules and salts. In view of this, Apfel et al. in US
15 patents 5,495,108 and 5,750,988 describe apparatuses for API
16 sources wherein the axis of the bore of the capillary 110 is at an
17 angle of 90° with respect the axis of the bore of the spray needle
18 111, as depicted in FIG. 3. According to Apfel et al., certain
19 experimental conditions lead to the production of large droplets by
20 the spray needle. These large droplets will move away from the
21 spray needle along the axis of the sprayer. However, an electric

1 field between the spray needle and the capillary will cause ions
2 formed from the spray to move towards the capillary. In this way,
3 the ions are separated from the spray droplets and the droplets do
4 not enter the capillary. However, this orientation is fixed in the
5 prior art source of Apfel. To change this orientation, one would
6 have to move the spray needle.

7 Prior art capillaries are further limited in the geometry of
8 the capillary bore. That is, prior art capillaries, as depicted in
9 FIGs. 1-3, are substantially straight (i.e., cylindrically
10 symmetric) and fixed (i.e., the geometry of the capillary and its
11 bore is fixed at the time of manufacture).

12 Applicant has recognized the need for an ion transfer device
13 or capillary which can be cleaned or replaced without the need to
14 shut down the entire mass spectrometer in which it resides. The
15 present invention allows for the removal of one or more sections of
16 the capillary (for cleaning or replacement) without having to shut
17 down the pumping system or the instrument to which it is attached.
18 In addition, the capillary according to the present invention can,
19 among other things, be made from different materials, take on
20 different sizes, shapes or forms, as well as perform different
21 functions.

1 The design of the multiple part capillary according to the
2 present invention provides added versatility to the use of
3 ionization chambers as well as to the use and performance of any
4 new and existing ionization methods. Furthermore, the invention
5 provides for interfacing with robotic sampling devices to provide
6 a fully automated system for the analysis of a variety of chemical
7 species efficiently and cost effectively.

8
9 SUMMARY OF THE INVENTION

10 The present invention relates generally to mass spectrometry
11 and the analysis of chemical samples, and more particularly to
12 capillaries for use therein. The invention described herein
13 comprises an improved method and apparatus for transporting ions
14 from a first pressure region in a mass spectrometer to a second
15 region therein. More specifically, the present invention provides
16 a multiple part capillary for more efficient use in mass
17 spectrometry (particularly with ionization sources) to transport
18 ions from the first pressure region to a second pressure region.

19 A first aspect of the present invention is to provide a
20 capillary for use in an ion source having improved flexibility and
21 accessibility over prior art designs. A capillary according to the

1 invention consists of at least two sections joined together end to
2 end such that gas and sample material in the gas can be transmitted
3 through the capillary across a pressure differential. The
4 capillary is intended for use in an ion source wherein ions are
5 produced at an elevated pressure and transported by the capillary
6 into a vacuum region of the source.

7 The present invention allows for the removal of one or more
8 sections of the capillary (for cleaning or replacement) without
9 having to shut down the pumping system of the instrument to which
10 it is attached. These sections may be made of different materials
11 -- e.g., glass, metal, composite, etc. -- which may be either
12 electrically conducting or non-conducting. Also, each section of
13 the capillary according to the invention does not have to be
14 straight or rigid, rather, one or more of the sections may be
15 flexible such that it (or they) can bend in any direction.

16 A further object of the invention is to provide a multiple
17 part capillary which offers improved flexibility in its geometric
18 orientation with respect to other devices in the ionization source
19 -- especially the ion production means. For example, the axis of
20 the bore or "channel" of the capillary at the capillary entrance
21 might be positioned at any angle with respect to the ion production

1 means. This angle, as discussed in Apfel U.S. Patent Nos.
2 5,495,108 and 5,750,988 can be important, for example, in the
3 separation of spray droplets from desolvated analyte ions. Also
4 according to the present invention, the entrance section of the
5 capillary might be modified or exchanged before or during
6 instrument operation to effect a change in the orientation of the
7 entrance with respect to the ion production means or other device.

8 This flexibility applies to the translational position of the
9 entrance of the capillary as well as its angular orientation. That
10 is, the position of the entrance of the capillary might be changed
11 before or during instrument operation by either modification or
12 exchange of the first section of the capillary. This allows for
13 the transmission of ions from a variety of locations either near or
14 removed from the immediate location of the source.

15 Another object of the present invention is to provide a
16 multipurpose multiple part capillary wherein the bore or "channel"
17 of one or more of the sections of the multiple part capillary may
18 comprise any useful geometry (i.e., straight, helical, wave-like,
19 etc.). For instance, it may be particularly useful to have an
20 inner channel of helical geometry. This will cause larger
21 particles (e.g., droplets from electrospray) to collide with the

1 walls of the capillary, while allowing smaller particles (e.g.,
2 fully desolvated electrosprayed ions) to pass through the
3 capillary. Note that the geometry of the bore may be, but is not
4 necessarily, related to the outer surface of the capillary. That
5 is, a capillary might have a cylindrically symmetric outer surface
6 but have an inner bore which is helical.

7 Yet another purpose of the present invention is to provide a
8 simple and efficient method and apparatus for integrating two
9 source assemblies. A complete ion source may include a multitude
10 of sub-assemblies. For example, an ion source might include an ion
11 production means sub-assembly and vacuum sub-assembly. The ion
12 production means sub-assembly might include a spray needle, its
13 holder, a translation stage, etc. The vacuum sub-assembly might
14 contain pumps, pumping restrictions, and ion optics for guiding
15 ions into the mass analyzer. In prior art sources and instruments,
16 the capillary would be integrated entirely in one sub-assembly --
17 the vacuum sub-assembly. As a result, significant effort is
18 required in prior art systems to align the ion production means
19 sub-assembly -- specifically the spray needle -- with the vacuum
20 sub-assembly -- specifically the capillary entrance. The multiple
21 part capillary according to the present invention eases the

1 integration of such sub-assemblies by including capillary sections
2 in each of the sub-assembly. The sub-assemblies are integrated by
3 joining the capillary sections together. Any necessary alignments
4 are performed within a given sub-assembly -- e.g. alignment of the
5 spray needle with the first section of capillary.

6 It is a further purpose of the present invention to provide
7 flexibility when using a particular mass spectrometer by providing
8 efficient use of a plurality of ionization sources. For example,
9 in combination with the ionization chamber described in a co-
10 pending application entitled Ionization Chamber For Atmospheric
11 Pressure Ionization, the present invention provides added
12 flexibility for switching from one ionization source to another or
13 from one sample to another. Specifically, the capillary according
14 to the invention is capable of efficiently and accurately being
15 used with multiple electrospray sources. In addition, the
16 capillary according to the invention is useful in multiplexing.

17 Another purpose of the invention is to provide a multiple part
18 capillary which can be used with chromatographic sample preparation
19 (e.g., liquid chromatography, capillary electrophoresis, etc.).
20 The effluent from such a chromatographic column may be injected
21 directly or indirectly into one of the sprayers. A plurality of

1 such chromatographic columns may be used in conjunction with a
2 plurality of sprayers -- for example one sprayer per column. The
3 presence of analyte in the effluent of any given column might be
4 detected by any appropriate means, for example a UV detector. When
5 analyte is detected in this way, the sprayer associated with the
6 column in question is "turned on" so that while analyte is present
7 the sprayer is producing ions but otherwise the sprayer does not.
8 If analyte is present simultaneously at more than one sprayer, the
9 sprayers are multiplexed, as discussed above.

10 Other objects, features, and characteristics of the present
11 invention, as well as the methods of operation and functions of the
12 related elements of the structure, and the combination of parts and
13 economies of manufacture, will become more apparent upon
14 consideration of the following detailed description with reference
15 to the accompanying drawings, all of which form a part of this
16 specification.

17 18 BRIEF DESCRIPTION OF THE DRAWINGS

19 A further understanding of the present invention can be
20 obtained by reference to a preferred embodiment set forth in the
21 illustrations of the accompanying drawings. Although the

1 illustrated embodiment is merely exemplary of systems for carrying
2 out the present invention, both the organization and method of
3 operation of the invention, in general, together with further
4 objectives and advantages thereof, may be more easily understood by
5 reference to the drawings and the following description. The
6 drawings are not intended to limit the scope of this invention,
7 which is set forth with particularity in the claims as appended or
8 as subsequently amended, but merely to clarify and exemplify the
9 invention.

10 For a more complete understanding of the present invention,
11 reference is now made to the following drawings in which:

12 FIG. 1 shows a partial cut-away cross-sectional view of a
13 prior art capillary comprising a unitary glass tube having a
14 cylindrical outer surface and internal bore;

15 FIG. 2 shows a partial cut-away cross sectional view of
16 another prior art capillary comprising a concentric outer capillary
17 sleeve and inner capillary tube;

18 FIG. 3 shows a prior art spray chamber of a prior art
19 electrospray ionization source wherein the channel of the spray
20 needle is oriented orthogonal to the channel of the capillary;

21 FIG. 4 shows a preferred embodiment of a multiple part

1 capillary according to the present invention;

2 FIG. 5 shows an alternate embodiment of the multiple part
3 capillary, wherein the channel of the first section comprises a
4 helical structure;

5 FIG. 6 shows an ESI sprayer needle oriented at an angle θ with
6 respect to the inlet to the channel and an angle α with respect to
7 the body of an embodiment of the multiple part capillary according
8 to the present invention;

9 FIG. 7 shows an embodiment of the multiple part capillary
10 according to the present invention as used with an ESI ionization
11 source;

12 FIG. 8 shows a multiple part capillary according to the
13 present invention as a means for integrating two source sub-
14 assemblies;

15 FIG. 9 shows the multiple part capillary according to the
16 present invention as a means for integrating a sample preparation
17 robot with an API source for mass spectrometry;

18 FIG. 10 shows an embodiment of the multiple part capillary
19 according to the present invention as a means for integrating a
20 sample preparation robot with an elevated pressure MALDI source for
21 mass spectrometry; and

1 FIG. 11 shows a close-up view of the use of the multiple part
2 capillary with a MALDI probe in accordance with the present
3 invention.

4
5 DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

6 As required, a detailed illustrative embodiment of the
7 present invention is disclosed herein. However, techniques,
8 systems and operating structures in accordance with the present
9 invention may be embodied in a wide variety of sizes, shaped,
10 forms and modes, some of which may be quite different from those
11 in the disclosed embodiment. Consequently, the specific
12 structural and functional details disclosed herein are merely
13 representative, yet in that regard, they are deemed to afford the
14 best embodiment for purposes of disclosure and to provide a basis
15 for the claims herein which define the scope of the present
16 invention.

17 The following presents a detailed description of a preferred
18 embodiment of the present invention, as well as some alternate
19 embodiments of the invention. As discussed above, the present
20 invention relates generally to the mass spectroscopic analysis of
21 chemical samples and more particularly to mass spectrometry.

1 Specifically, an apparatus and method are described for transport
2 of ions between pressure regions within a mass spectrometer.
3 Reference is herein made to the figures, wherein the numerals
4 representing particular parts are consistently used throughout
5 the figures and accompanying discussion.

6 With reference first to FIG. 4, shown is multiple part
7 capillary 35 according to a preferred embodiment of the present
8 invention. As depicted in FIG. 4, multiple part capillary 35
9 comprises: first section 28 having capillary inlet end 26 and
10 first channel 27; union 29 having o-ring 31; second section 33
11 having second channel 32 and capillary outlet end 34; and metal
12 coatings 30A and 30B. According to the preferred embodiment,
13 first section 28 is connected to second section 33 by union 29.
14 In the preferred embodiment, union 29 is substantially
15 cylindrical having two coaxial bores, 60 and 61, and through hole
16 62 of the same diameter as channels 26 and 32. In the preferred
17 embodiment, section 28 and union 29 are composed of metal - e.g.
18 stainless steel. The inner diameter of bore 60 and the outer
19 diameter of section 28 are chosen to achieve a "press fit" when
20 section 28 is inserted into bore 60. Because the press fit is
21 designed to be tight, union 29 is thereby strongly affixed to

1 section 28 and a gas seal is produced between union 29 and
2 section 28 at the surface of the bore. The inner diameter of
3 bore 61 is of slightly larger diameter than the outer diameter of
4 section 33 (including metal coating 30A) so as to produce a "slip
5 fit" between union 29 and section 33. A gas seal is established
6 between bore 61 and section 33 via o-ring 31. Electrical contact
7 between metal coating 30A, union 29, and section 28 via direct
8 physical contact between the three. Through hole 62 allows for
9 the transmission of gas from entrance end 26 through to exit end
10 34 of the capillary. Ideally, union 29 and sections 28 and 33
11 are formed in such a way as to eliminate any "dead volume"
12 between these components. To accomplish this, the ends of
13 sections 28 and 33 are formed to be flush with the inner surface
14 of union 29. Note that the body of section 33 - excluding metal
15 coatings 30A and 30B - is composed of glass in the preferred
16 embodiment. As a result, metal coating 30A - together with union
17 29 and section 28 - can be maintained at a different electrical
18 potential than metal coating 30B.

19 Alternatively, union 29, and sections 28 and 33 may be
20 composed of a variety of materials conducting or non-conducting;
21 the outer diameters of the sections may differ substantially from

1 one another; the inner diameters of the sections may differ
2 substantially from one another; either or both ends or any or all
3 sections may be covered with a metal or other coating; rather
4 than a coating, the ends or capillary sections may be covered
5 with a cap composed of metal or other material; the capillary may
6 be composed of more than two sections always with one fewer union
7 than sections; and the union may be any means for removably
8 securing the sections of capillary together and providing an
9 airtight seal between these sections.

10 Each end of union 29 could comprise a generally cylindrical
11 opening having an internal diameter slightly larger than the
12 external diameter of the end of the capillary section which is to
13 be inserted therein. In such an embodiment, a gas seal is made
14 with each capillary section via an o-ring similar to o-ring 31.
15 As a further alternative, one might use springs to accomplish
16 electrical contact between union 29 and sections 28 and 33. In
17 this case a conducting spring would be positioned in union 29
18 adjacent to o-ring 31.

19 Moreover, in a preferred embodiment of the capillary
20 according to the invention, the length of first section 28 is
21 less than (even substantially less than) the length of second

1 section 33. More specifically, the dimensions of first section
2 28 and second section 33 are such that within a range of desired
3 pressure differentials across capillary 35, a gas flow rate
4 within a desired range will be achieved. For example, the length
5 of second section 33 and the internal diameter of second channel
6 32 are such that the gas transport across second section 33 alone
7 (i.e., with first section 28 removed) at the desired pressure
8 differential will not overload the pumps which generate the
9 vacuum in the source chamber of the system. This allows the
10 removal (e.g., for cleaning or replacement) of first section 28
11 of capillary 35 without shutting down the pumping system of the
12 mass spectrometer.

13 While the prior art, as depicted in FIG. 2, attempts to
14 accomplish removal, without shutting down the vacuum, it is
15 difficult and cumbersome. As discussed previously, tools and
16 adhesives may be required to remove and replace the capillary.
17 The multiple part capillary according to the present invention
18 provides a much simpler method and apparatus for accomplishing
19 this result (i.e., without the use of adhesives, tools, etc.).

20 Turning next to FIG. 5, an alternate embodiment of capillary
21 35 is shown wherein capillary section 28 has a serpentine

1 internal channel 64. That is, the geometric structure of the
2 internal channel of the capillary section is sinusoidal. Of
3 course, other geometrical structures (i.e., helical, varying
4 diameter, non-uniform, etc.) may be used in accordance with the
5 invention. Having sinusoidal internal channel 64 causes larger
6 particles -- such as droplets from an electrospray -- to collide
7 with the walls of the channel and thereby not pass completely
8 through the capillary. On the other hand, smaller particles --
9 such as fully desolvated electrosprayed ions -- do not collide
10 with the walls and pass completely through the capillary. The
11 curved (or sinusoidal) geometry of channel 64 also increases the
12 length of the channel, which provides the advantage of permitting
13 a larger diameter channel. Such a larger diameter channel may be
14 advantageous in that it may provide greater acceptance of sampled
15 species (e.g., electrosprayed ions, etc.) at a given flow rate
16 and pressure differential. Alternatively, a sinusoidal -- or any
17 other geometry -- channel may be used in either first section 28
18 or second section 33, or both.

19 In accordance with the present invention, it is observed
20 that the introduction of ions from an ionization means into the
21 multiple part capillary of the invention may be accomplished at

1 any angle of incidence between the ionization means and the inlet
2 of the capillary. Referring now to FIG. 6, shown is an
3 embodiment of the multiple part capillary according to the
4 invention as used with an ESI sprayer 65 wherein axis 70 of
5 sprayer 65 is oriented at angle α 66 with respect to axis 69 of
6 the body of capillary 72. However, because channel 73 of
7 capillary section 74 is curved, angle θ 67 between sprayer axis
8 70 and axis 71 of channel entrance 68 can be substantially
9 different than angle α 66. The embodiment shown in FIG. 6
10 demonstrates that the capillary entrance angle α 66 may be any
11 angle from 0° and 180° . The specific angle selected is dependent
12 upon, among other things, the sample species being tested, the
13 ionization source used, etc. As discussed above, the
14 electrospray process results in the formation of charged droplets
15 and molecular ions. The presence of large droplets in the spray
16 can result in contamination of the capillary and generally poor
17 instrument performance. One way of limiting the influence of
18 large droplets on instrument performance is to spray away from
19 the capillary entrance. That is, the spray needle is oriented so
20 that it is not pointed directly at the capillary entrance. Large
21 droplets formed in a source with such a geometry will tend to

1 move along the axis of the spray needle and not enter the
2 capillary, whereas desolvated ions will be attracted to the
3 capillary entrance by the electrostatic field between the spray
4 needle and the capillary. Thus, in the embodiment of figure 6,
5 smaller angles α 66 and θ 67 will tend to reduce the fraction of
6 droplets that enter the capillary.

7 In any case, the sinusoidal geometry of channel 73 tends to
8 limit the contamination of capillary 72 due to large droplets to
9 section 74. Large droplets which enter the capillary will tend
10 to strike the walls of channel 73 and not pass through to section
11 33. Section 74 can be removed from the system - by pulling it
12 off along axis 69 - and cleaned without necessarily shutting the
13 instrument or its vacuum system off.

14 Depicted in FIG. 7 is an ionization source which
15 incorporates the multiple part capillary of the invention where
16 the ion production means is an ESI sprayer device, shown as spray
17 needle 36 in spray chamber 40. During normal operation of a
18 preferred embodiment with an ESI source, sample solution is
19 formed into droplets at atmospheric pressure by spraying the
20 sample solution from spray needle 36 into spray chamber 40. The
21 spray is induced by the application of a high potential between

1 spray needle 36 and entrance 26 of first capillary section 28
2 within spray chamber 40. Sample droplets from the spray
3 evaporate while in spray chamber 40 thereby leaving behind an
4 ionized sample material (i.e., sample ions). These sample ions
5 are accelerated toward capillary inlet 26 of channel 27 by an
6 electric field generated between spray needle 36 and inlet 26 of
7 first section 28 of capillary 35. These ions are transported
8 through first channel 27 into and through second channel 32 to
9 capillary outlet 34. As described above with regard to FIG. 4,
10 first section 28 is joined to second section 33 in a sealed
11 manner by union 29. The flow of gas created by the pressure
12 differential between spray chamber 40 and first transfer region
13 45 further causes the ion to flow through the capillary channels
14 from the ionization source toward the mass analyzer.

15 Still referring to FIG. 7, first transfer region 45 is
16 formed by mounting flange 48 on source block 54 where a vacuum
17 tight seal is formed between flange 48 and source block 54 by o-
18 ring 58. Capillary 35 penetrates through a hole in flange 48
19 where another vacuum tight seal is maintained (i.e., between
20 flange 48 and capillary 35) by o-ring 56. A vacuum is then
21 generated and maintained in first transfer 45 by a pump (e.g., a

1 roughing pump, etc., not shown). The inner diameter and length
2 of capillary 35 and the pumping speed of the pump are selected to
3 provide as high a rate of gas flow through capillary 35 as
4 reasonably possible while maintaining a pressure of 1 mbar in the
5 first transfer region 45. A higher gas flow rate through
6 capillary 35 will result in more efficient transport of ions.

7 Next, as further shown in FIG. 7, first skimmer 51 is placed
8 adjacent to capillary exit 34 within first transfer region 45.
9 An electric potential between capillary outlet end 34 and first
10 skimmer 51 accelerates the sample ions toward first skimmer 51.
11 A fraction of the sample ions then pass through an opening in
12 first skimmer 51 and into second pumping region 43 where pre-
13 hexapole 49 is positioned to guide the sample ions from the first
14 skimmer 51 to second skimmer 52. Second pumping region 43 is
15 pumped to a lower pressure than first transfer region 45 by pump
16 53. Again, a fraction of the sample ions pass through an opening
17 in second skimmer 52 and into third pumping region 44, which is
18 pumped to a lower pressure than second pumping region 43 via pump
19 53.

20 Once in third pumping region 44, the sample ions are guided
21 from second skimmer 52 to exit electrodes 55 by hexapole 50.

1 While in hexapole 50 ions undergo collisions with a gas (i.e., a
2 collisional gas) and are thereby cooled to thermal velocities.
3 The ions then reach exit electrodes and are accelerated from the
4 ionization source into the mass analyzer for subsequent analysis.

5 Another purpose of the present invention is to provide a
6 simple and efficient method and apparatus for integrating two
7 source assemblies. As depicted in figure 8, a complete ion source
8 may include a multitude of sub-assemblies. For example, ion source
9 80 includes ion production means sub-assembly 81 and vacuum sub-
10 assembly 82. The ion production means sub-assembly includes, among
11 other things, spray chamber 40 and spray needle 36. The vacuum sub-
12 assembly includes among other things, pump 53, pumping restrictions
13 51 and 52, and ion optical elements 49 - 52 and 55 for guiding ions
14 into the mass analyzer. In prior art sources and instruments, the
15 capillary would be integrated entirely in one sub-assembly - the
16 vacuum sub-assembly. As a result, significant effort is required
17 in prior art systems to align the ion production means sub-assembly
18 - specifically the spray needle - with the vacuum sub-assembly -
19 specifically the capillary entrance. The multiple part capillary
20 according to the present invention can be used to ease the
21 integration of such sub-assemblies by including capillary sections

1 in each of the sub-assembly. In the embodiment of figure 8,
2 capillary section 28 is an integral component of ion production
3 means sub-assembly 81 and capillary section 33 is an integral
4 component of vacuum sub-assembly 82. Sub-assemblies 81 and 82 are
5 integrated in part by joining capillary sections 28 and 33 together
6 via union 29. Any necessary alignments are performed within a given
7 sub-assembly - e.g. alignment of spray needle 36 with entrance 26
8 of channel 27. In alternate embodiments, any variety of sub-
9 assemblies might be integrated, in part or in whole, by including
10 capillary sections in these sub-assemblies and subsequently joining
11 these capillary sections together as discussed with respect to
12 figure 8. Further, any number of sub-assemblies with any variety
13 of functions might be used. Such functions might include ion
14 production, desolvation of spray droplets via a heated capillary
15 section, ion transfer to the mass analyzer, etc. Clearly, any type
16 of atmospheric pressure ionization means - including ESI, API
17 MALDI, atmospheric pressure chemical ionization, nano electrospray,
18 pneumatic assist electrospray, etc. - could be assembled into a
19 source in this way.

20 The capillary according to the present invention might also
21 be used to transport ions from ionization means remote from the

1 instrument. This is exemplified by the embodiment of FIG. 9.
2 Shown in FIG. 9 is an embodiment of the multiple part capillary
3 according to the invention as used for integrating a sample
4 preparation robot with an Atmospheric Pressure Ionization (API)
5 source. Specifically, the system shown comprises, among other
6 things: robot 90; robot arm 91; sample tray (not shown); source
7 tray 92; sprayer 93; multiple part capillary 98 comprising first
8 section 28 having inlet 26, second section 33 having outlet 34,
9 and union 29; gas transport line 94; source cover 95; ~~source~~
10 vacuum sub-assembly 96; and mass analyzer 97.

11 Robots such as in the embodiment of FIG. 9 - for example, a
12 Gilson 215 Liquid Handler Robot - consist of a robot arm - e.g.
13 arm 91 - used to manipulate samples, and "trays" of samples and
14 sample containers. The robot arm is used to move samples,
15 solutions, and reactants from one container - i.e. tubes, vials,
16 or microtiter wells - to another. By mixing analyte, solvents,
17 and reactants in a predefined way, the robot can be used to
18 prepare samples for subsequent analysis. As depicted in FIG. 9,
19 sample spray and ionization would occur within robot 90 and only
20 ions would be transported -- via multiple part capillary 98 -- to
21 mass analyzer 97. In the particular embodiment shown, a

1 specially prepared source tray 92 is used. Sample is obtained by
2 robot 90 from a sample tray by sucking solution into sprayer 93.
3 Robot arm 91 then moves sprayer 93 to source tray 92 and to a
4 predefined location near entrance 26 of capillary 98. Drying gas
5 can be transported into source tray from vacuum sub-assembly 96
6 via a gas transport line 94. Sprayer 93 is attached to robot arm
7 91 and set at ground potential (of course, any ESI sprayer may be
8 used (e.g., pneumatically assisted sprayers, nanosprayer needles,
9 etc.)), while inlet 26 to first section 28 of capillary 98 set at
10 high voltage. This potential difference between sprayer 94 and
11 first section 28 induces the spray of the sample solution and
12 production of analyte ions.

13 The capillary according to the present invention is also
14 useful in transporting ions from varying locations during
15 operation. Turning to FIG. 10, shown is an embodiment of the
16 multiple part capillary according to the invention as a means for
17 integrating a sample preparation robot with an elevated pressure
18 MALDI source for use in mass spectrometry. The system depicted
19 in FIG. 10 comprises a laser 99, attenuator 100, fiber optic 101,
20 robot 90 having robot arm 91 for control and movement of sample
21 probe 102, MALDI sample tray 103, sample holder 104, alternative

1 embodiment of capillary 98 having first section 105, second
2 section 33 joined by union 29, ionization source cover 95, vacuum
3 sub-assembly 96, and mass analyzer 97.

4 The alternative embodiment of the multiple part capillary of
5 the invention as shown in FIG. 10 comprises a flexible first
6 section 105 such that its inlet end may be moved by robot arm 68
7 91 to various positions for acceptance of the MALDI samples to be
8 analyzed. As depicted in FIG. 10, sample preparation and
9 ionization are both performed by robot 90 such that only ions
10 would be transported through the multiple part capillary 98 to
11 vacuum sub-assembly 96 and ultimately to mass analyzer 97.
12 Specifically, robot arm has attached at its end sample probe 102,
13 and fiber optic 101 for directing the laser beam from laser 99
14 onto sample holder 104 to ionize samples thereon. The ions
15 formed by the laser beam hitting the samples on sample holder 104
16 are then carried by the gas flow into and through capillary 98 to
17 the differential pumping region of vacuum sub-assembly 96, where
18 additional ion optics (not shown) are designed to further
19 transport the ions from outlet end of capillary 98 to mass
20 analyzer 97 for subsequent analysis.

21 As shown in FIG. 11, which depicts an embodiment of the

multiple part capillary for use with a MALDI probe, the multiple part capillary according to the invention provides a means for integrating a sample preparation robot with MALDI mass analysis. Shown in FIG. 11 are capillary 105, robot arm 91, receptacle 106, fiber optic 101, and sample plate 104 with raised conical formations 107 onto which samples (not shown) are deposited. Sample plate 104 and the conical formations form a unitary device composed of conducting material - e.g. stainless steel. In this alternate embodiment, capillary section 105 optionally comprises a specially shaped orifice which fits over cone-shaped sample holder formations 107 (one at a time) in such a way that gas flowing through capillary 98 readily captures the ions formed from the sample by laser desorption ionization. Optionally, a potential may be applied between sample carrier 104 and capillary 78 section 105 to help draw ions into the channel of capillary 78 section 105. Also, fiber optic 101 might be adjusted via piezo electrics or other mechanics to direct the laser beam to any region of the specific cone-shaped sample of samples 82 to be ionized. Optionally, this redirecting of the laser beam may occur during the ionization process such that the entire sample is ionized.

1 While the present invention has been described with
2 reference to one or more preferred embodiments, such embodiments
3 are merely exemplary and are not intended to be limiting or
4 represent an exhaustive enumeration of all aspects of the
5 invention. The scope of the invention, therefore, shall be
6 defined solely by the following claims. Further, it will be
7 apparent to those of skill in the art that numerous changes may
8 be made in such details without departing from the spirit and the
9 principles of the invention. It should be appreciated that the
10 present invention is capable of being embodied in other forms
11 without departing from its essential characteristics.
12

1 ABSTRACT

2 The present invention provides a multiple part capillary for
3 use in mass analysis instruments. Specifically, a multiple part
4 capillary comprising at least two capillary sections joined with
5 airtight seal by a union for use in mass spectrometry
6 (particularly with ionization sources) to transport ions between
7 pressure regions of a mass spectrometer for analysis is described
8 herein. Preferably, the capillary is useful to transport ions
9 from an elevated pressure ionization source to a first vacuum
10 region of a mass analysis system.

1 What is claimed is:

2

3 1. An apparatus for transporting ions from a first pressure
4 region to a second pressure region within a mass spectrometer,
5 wherein said apparatus comprises:

6 first and second capillary sections each having an
7 inlet end and an outlet end; and

8 a union having first and second openings;

9 wherein said outlet end of said first capillary section is
10 removably positioned within said first opening of said union, and
11 wherein said inlet of said second capillary section is removably
12 positioned within said second opening of said union.

13
14 2. An apparatus according to claim 1, wherein said first
15 section comprises a channel having a helical structure.

16

17 3. An apparatus according to claim 1, wherein said union
18 comprises means for removably securing said ends of said first
19 and second sections.

20

21 4. An apparatus according to claim 1, wherein said union

1 comprises means for providing an airtight seal between said ends
2 of said first and second sections within said union.

3 5. An apparatus according to claim 1, wherein said inlet ends
4 and said outlet ends comprise conductive end caps.

5
6 6. An apparatus according to claim 1, wherein said ions are
7 transported from an ionization source into a first vacuum region
8 of a mass spectrometer.

9
10 7. An apparatus according to claim 6, wherein said ionization
11 source is an API source.

12
13 8. An apparatus according to claim 6, wherein said ionization
14 source is an ESI device.

15
16 9. An apparatus according to claim 6, wherein said ionization
17 source is a pneumatic assisted electrospray source.

18
19 10. An apparatus according to claim 6, wherein said ionization
20 source is an electron impact source.

1 11. An apparatus according to claim 6, wherein said ionization
2 source is a chemical ionization source.

3
4 12. An apparatus according to claim 6, wherein said ionization
5 source is a matrix assisted laser desorption ionization source.

6
7 13. An apparatus according to claim 6, wherein said ionization
8 source is a plasma desorption source.

9
10 14. An apparatus according to claim 6, wherein said ionization
11 source uses liquid chromatography.

12
13 15. An apparatus according to claim 1, wherein said apparatus is
14 used to multiplex sample materials.

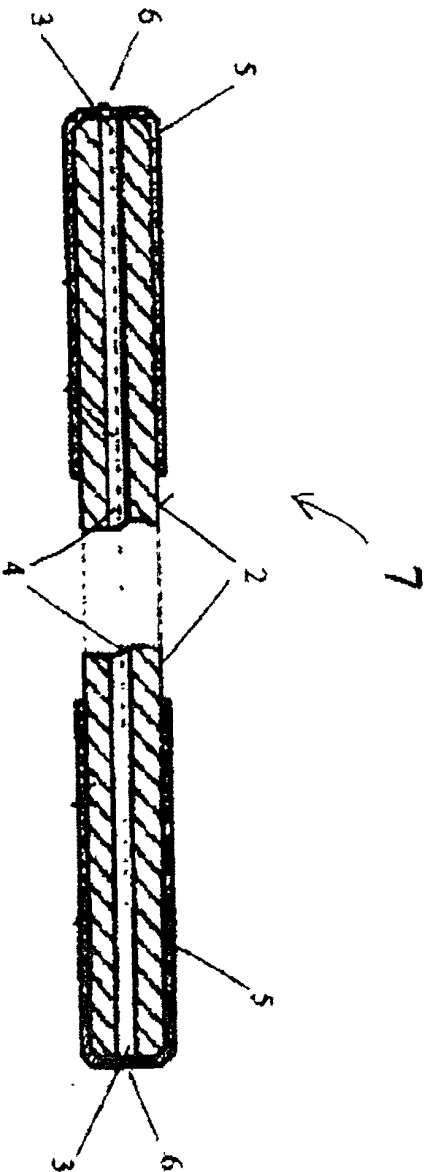


Figure 1

Prior Art

09507423 021300

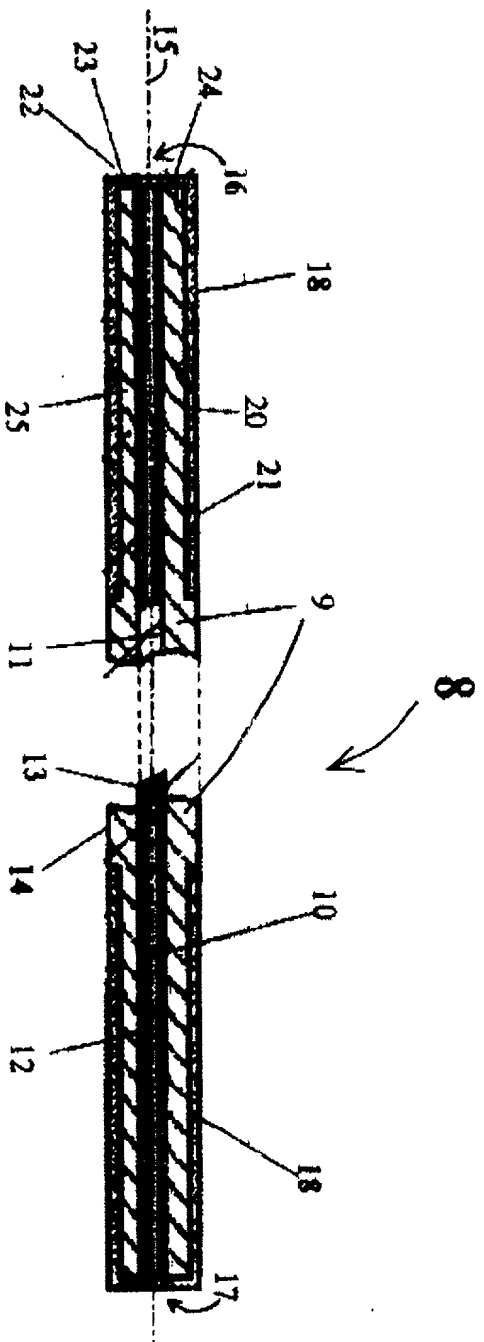
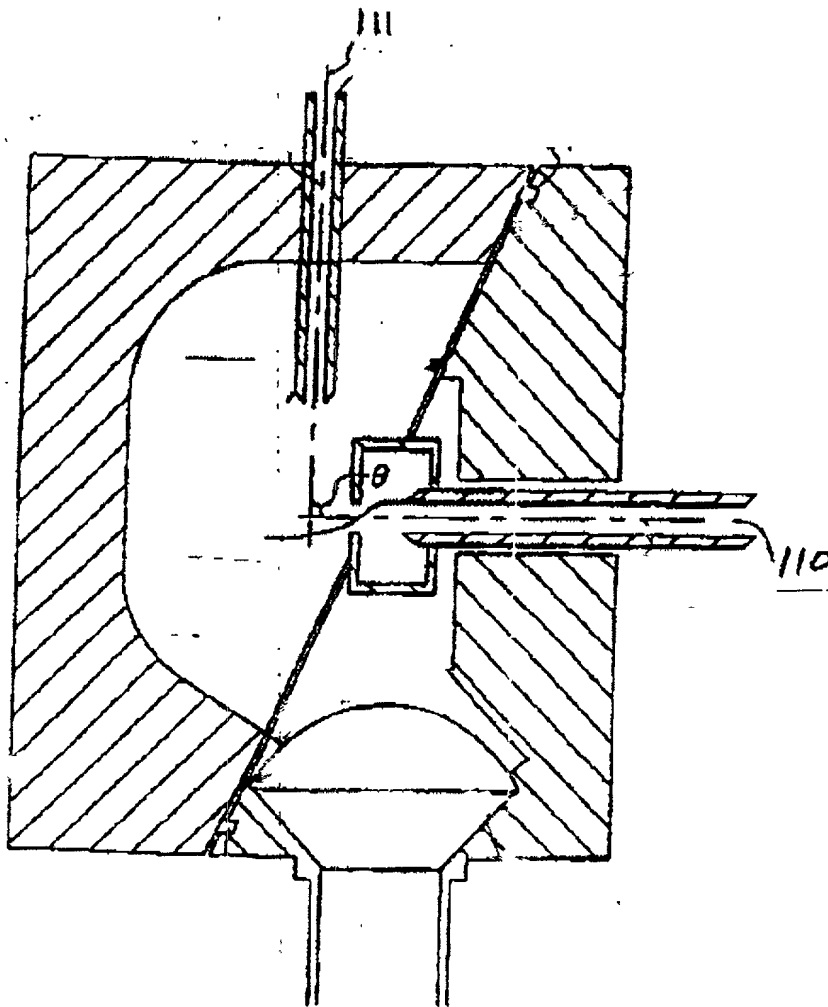


Figure 2
Prior Art

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Prior Art

FIG. 3

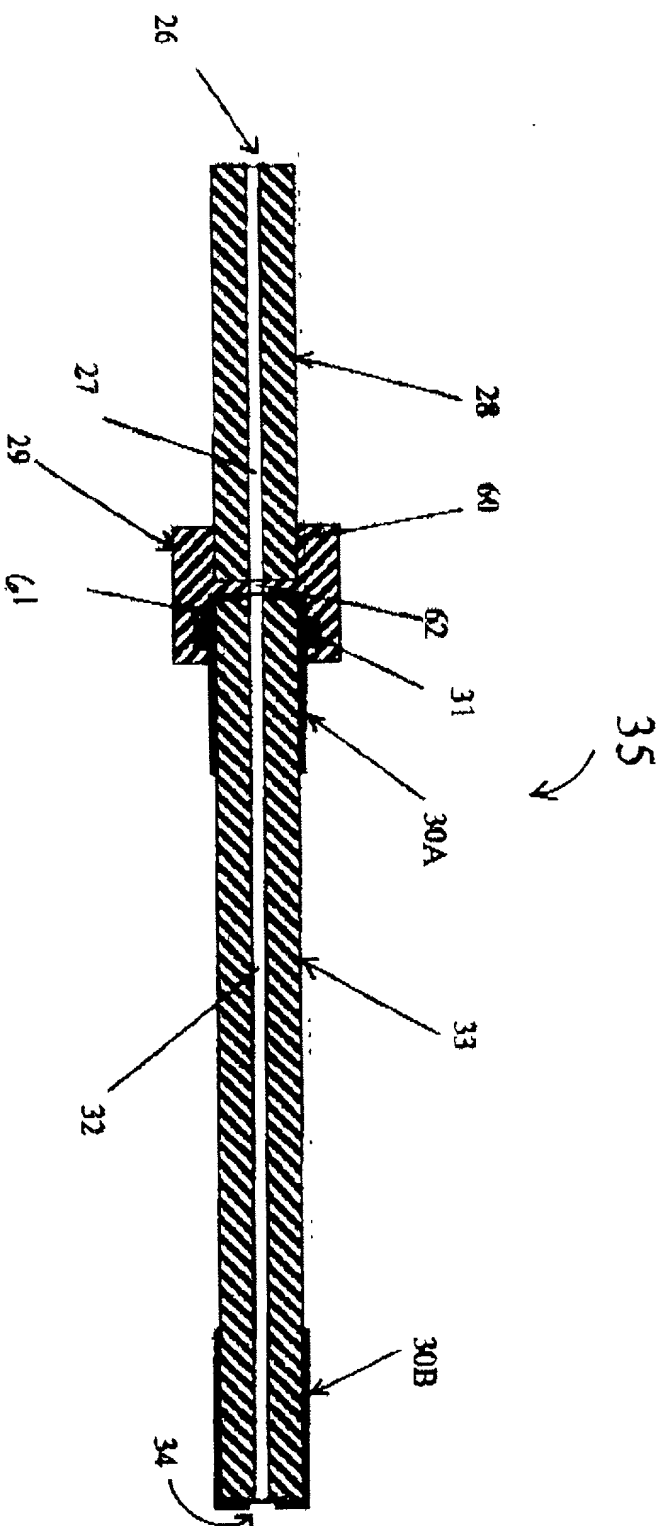


Figure 4

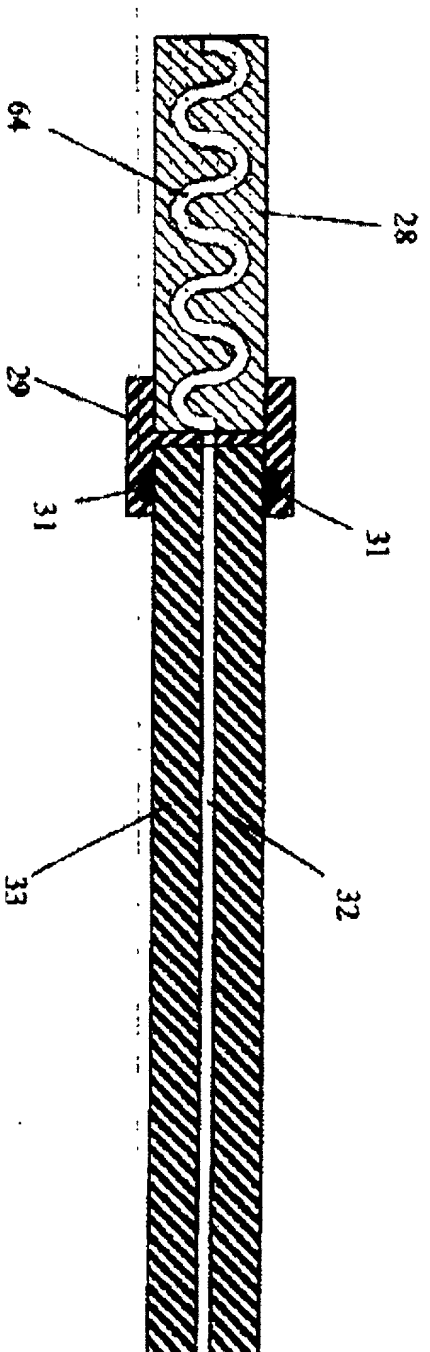


Figure 5

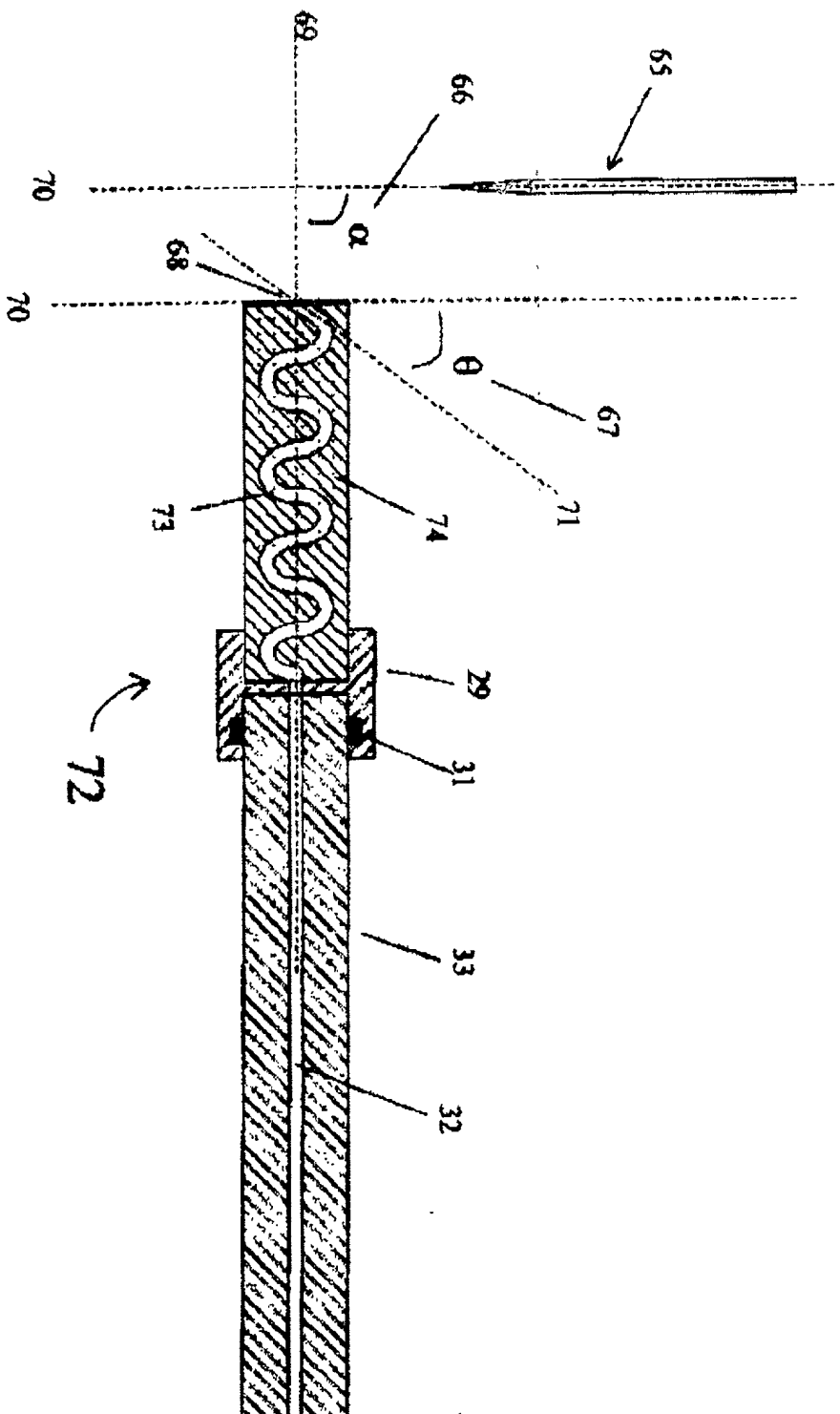


Figure 6

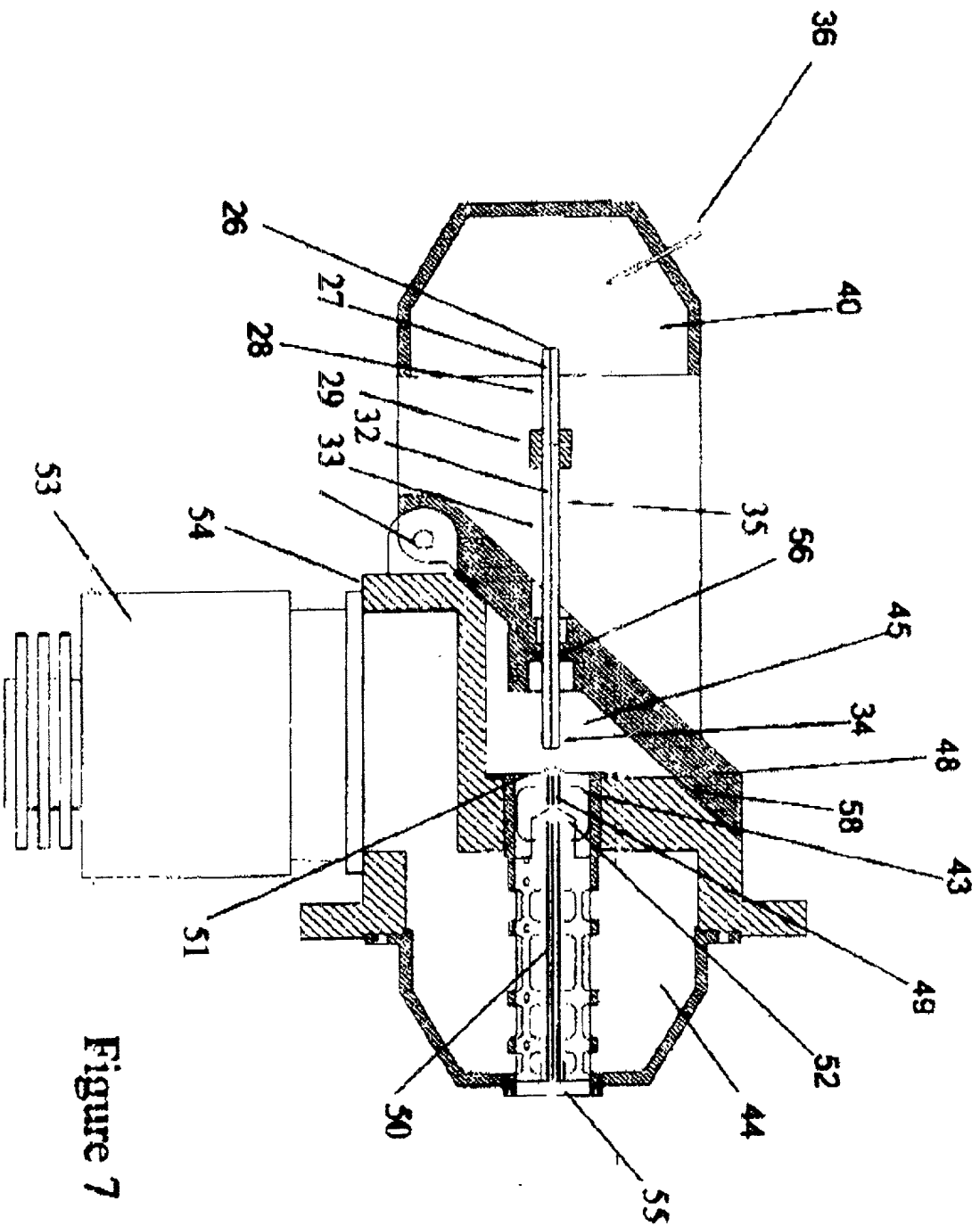


Figure 7

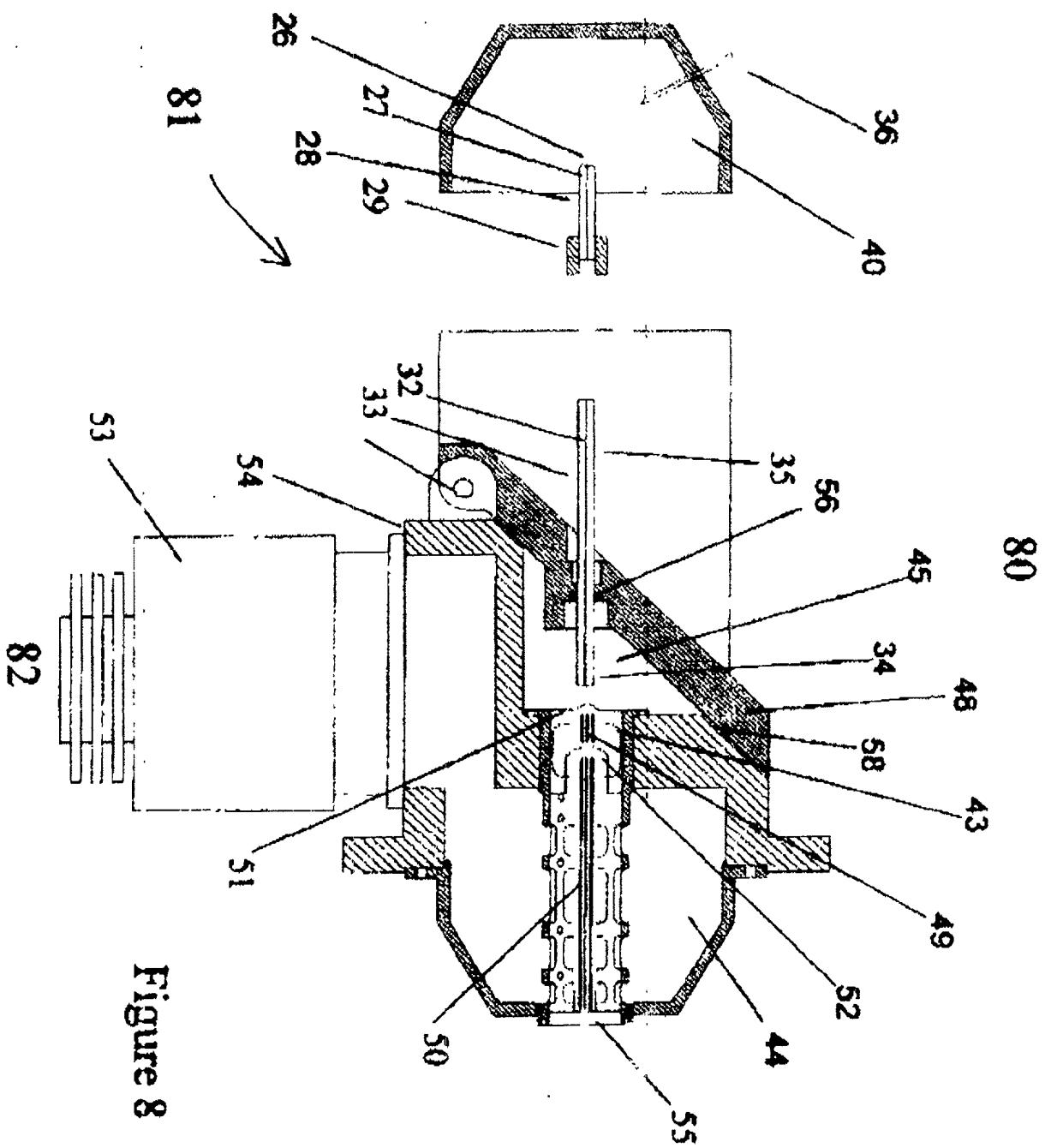


Figure 8

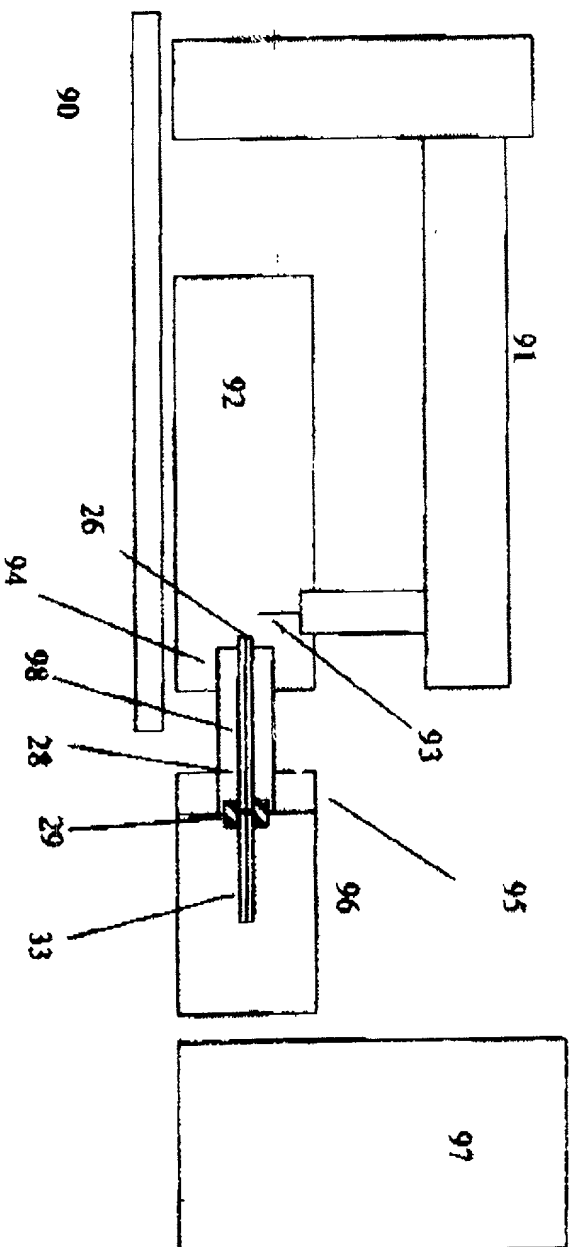


Figure 9

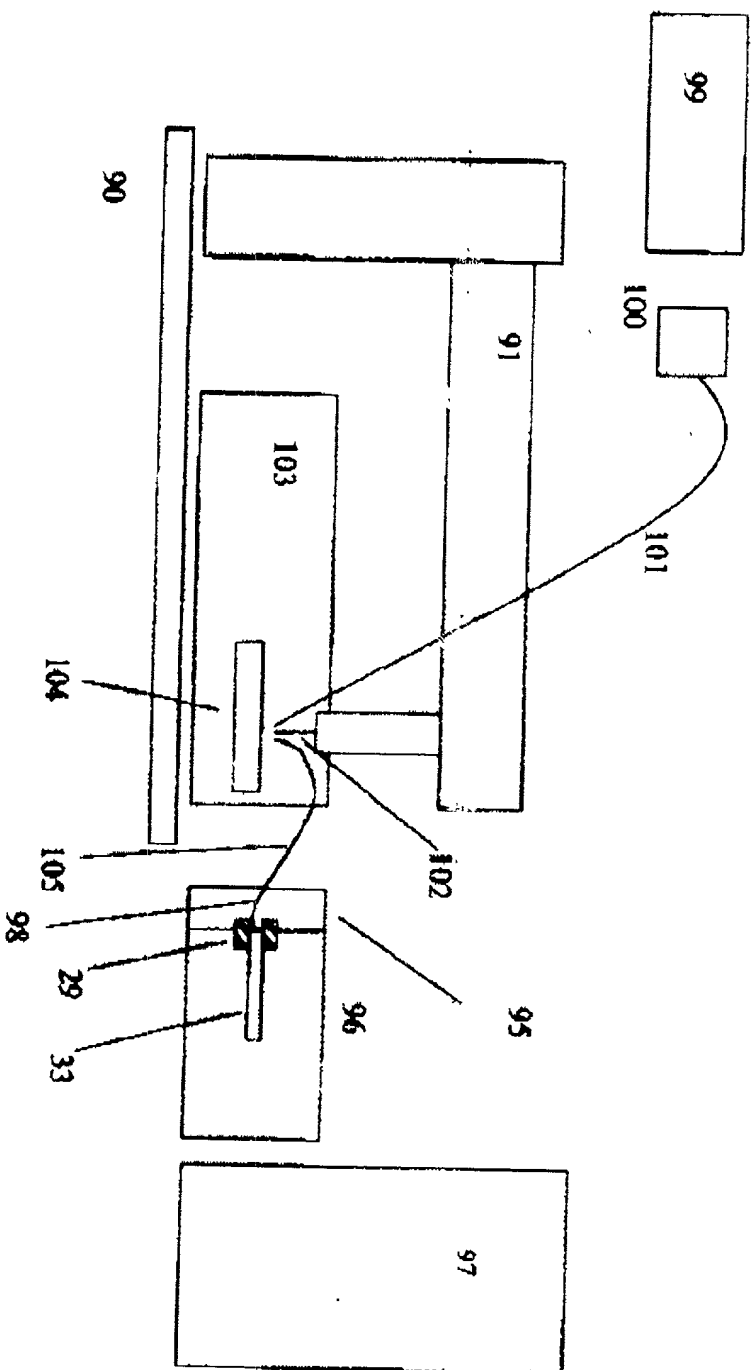


Figure 10

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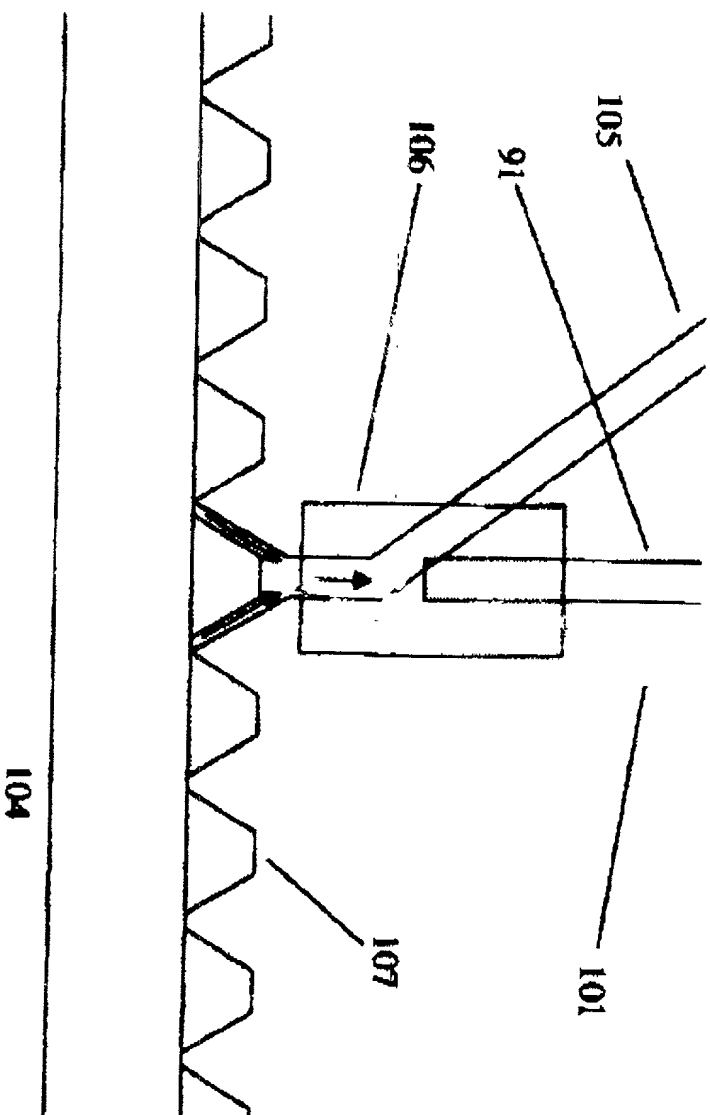


Figure 11

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below at 201 et seq. underneath my name.

I believe I am the original, first and sole inventor if only one name is listed at 201 below, or an original, first and joint inventor if plural names are listed at 201 et seq. below, of the subject matter which is claimed and for which a patent is sought on the invention entitled **METHOD AND APPARATUS FOR A MULTIPLE PART CAPILLARY DEVICE FOR USE IN MASS SPECTROMETRY**, the specification of which:

☒ is attached hereto ☐ was filed on _____ as Application Serial No. _____.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119/§172 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

EARLIEST FOREIGN APPLICATION(S), IF ANY, FILED PRIOR TO THE FILING DATE OF THE APPLICATION			
APPLICATION NUMBER	COUNTRY	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 U.S.C. 119/172
N/A			YES <input type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NO.	FILING DATE	STATUS		
		PATENTED	PENDING	ABANDONED

POWER OF ATTORNEY: As a named inventor, I hereby appoint John F. Ward (Reg. No. 33,811) and John W. Olivo, Jr. (Reg. No. 35,634), whose address is Ward & Olivo, 708 Third Avenue, New York, New York 10017, and each of them, my attorneys, to prosecute this application, and to transact all business in the Patent and Trademark Office connected therewith.

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	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
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	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
205	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE
206	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202	SIGNATURE OF INVENTOR 203
DATE	DATE	DATE
SIGNATURE OF INVENTOR 204	SIGNATURE OF INVENTOR 205	SIGNATURE OF INVENTOR 206
DATE	DATE	DATE